

REMARKS

In view of the following remarks, the Examiner is respectfully requested to allow Claims 1 to 28, the only claims pending and currently under examination in this application.

The Examiner is thanked for the helpful interview held with the undersigned and Dr. Bradley Galer on April 16, 2007. During the interview, the Peyman was reviewed in view of its teaching of intranasal administration of an opioid active agent. In addition, the above amendments were discussed and the Examiner acknowledged that the claims appeared to distinguish over the cited art. The Examiner indicated that the claims would be further reviewed upon filing of a response. It is believed that the above discussion provides an accurate summary of the substance of the interview.

Amendment to the Claims

Claims 1, 6 and 11 have been amended to change the transitional phrase to 'consisting of' and to include indomethacin responsive headaches in the list of indications, as supported by Claim 27. As no new matter has been added by way of these amendments, entry thereof by the Examiner is respectfully requested.

Claim Rejections - 35 U.S.C. § 103

Claims 1-28 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Peyman (U.S. Patent No. 5,855,907) in view of Geaney.

According to the MPEP § 706.02 (j), to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must

teach or suggest all the claim limitations.

An element of the rejected claims is the step of topically applying an effective amount of a topical NSAID formulation "to a keratinized skin surface of the head of said host."

The combined teaching of Peyman in view of Geaney fails to teach or suggest this claim element of applying the formulation to a keratinized skin surface of the head of said host.

One of skill in the art would read Peyman as teaching intranasal delivery of a formulation. One of skill in the art would so read Peyman because Peyman includes the following passage at Col. 4, lines 4 to 22:

It should be understood that "a migraine-ameliorating effective amount" refers to an amount of opioid which effects a prophylactic or therapeutic response in the patient in need of such a response over a reasonable time frame, causing either a diminution or an eradication of one or more of the symptoms of migraine. While the precise mechanism by which the topical administration of a migraine-ameliorating effective amount of an opioid relieves migraine is unknown, without limiting the invention to any particular theory, it is believed that the treatment is effective because the opioid affects the sphenopalatine ganglion ("SPG"). It is thus readily apparent to one skilled in the art that the effectiveness of topical application is correlated with maximizing the degree to which the opioid is absorbed and affects the SPG, and minimizing the degree to which the opioid is absorbed systemically. Thus, topical administration on and around the sinal cavity is preferred, including the administration of the opioid conjunctivally, intranasally, or transdermally in the region of the sinal cavity.

Since the target of the opioid is the SPG, and this nerve is accessible only through the nasal passage, one of skill in the art would read the phrase "topical administration" of Peyman as meaning through the nasal passage. Furthermore, the working exemplification in Peyman reports a study demonstrating intranasal application of 4% solution of lidocaine. In addition, the Summary of Invention (6th paragraph) reads:

"The invention provides methods of intranasal administration in the form of nose drops, nasal spray, gel, emulsion, and ointment. In a preferred embodiment, if the migraine is unilateral, nose drops are administered into the nostril on the same side of the head as the headache, or into both nostrils if the pain is bilateral."

As such, one of skill in the art would read Peyman as teaching solely intranasal delivery of an opioid formulation. Intranasal delivery is not delivery to a keratinized skin surface of the head of a subject as claimed. As such, Peyman is deficient in failing to teach or suggest the delivery of a topical NSAID formulation to a keratinized skin surface of a head of a host as claimed.

Geaney fails to make up this deficiency in Peyman because Geaney teaches only the oral administration of indomethacin to a host. Not only is the route of administration different than delivery of the drug via topical formulation to a keratinized skin surface of a head of a host as claimed, the site of activity is different as well. The oral route of administration of indomethacin will result in systemic activity, i.e. via the circulation the drug is delivered to the central nervous system, as compared to the topical drug delivery as claimed, whereby the drug is delivered regionally to the bodily tissues underlying the application skin site, i.e. local peripheral nerves and soft tissues.

Accordingly, the combined teaching of Peyman in view of Geaney fails to teach or suggest the claim element of delivering a topical NSAID formulation to a keratinized skin surface of a head of a host.

In addition, the claimed methods require that NSAID be the only active agent that is administered to the host to treat the headache. Peyman clearly teaches that his method is directed to administration of an opioid, which in certain embodiments may be administered in combination with antiinflammatory compound. However, in all embodiments of Peyman, the opioid is the essential active agent. As such, Peyman fails to teach or suggest a method in which a nonsteroidal antiinflammatory agent is the sole active agent that is administered to the subject, as claimed.

Accordingly, Peyman in view of Geaney fails to teach this element of the claimed methods as well.

As such, the combined teaching of Peyman in view of Geaney fails to teach or suggest all of the elements of the claimed methods. Accordingly, Claims 1 to 28 are not obvious under 35 U.S.C. § 103(a) over Peyman (U.S. Patent No. 5,855,907) in view of Geaney and this rejection may be withdrawn.

Claims 1 to 28 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over "Migraine Headaches" in view of Geaney.

As acknowledged by the Office, the article "Migraine Headaches" fails to teach the topical administration of an NSAID. To make up for this deficiency, the Examiner looks to Geaney.

However, as reviewed above, Geaney describes only the oral administration of Indomethacin and provides no teaching or suggestion of application of Indomethacin to a keratinized skin surface of a host. Nor does Geaney describe the utility of other NSAID drugs.

Furthermore, the agents employed in "Migraine Headaches," are clearly distinct from NSAIDS and any activity provided by these agents cannot reasonably be used to predict how NSAIDS will work upon application to a keratinized skin surface. The Migraine Headaches reference discloses "rubbing herbal medicinal formulation containing herbs to treat migraine into the forehead and temples." Herbals are not NSAIDs and have been categorized as 'counter-irritants' or rubrifaciants in the art. These agents have a different mechanism of action from NSAIDS and therefore any results achieved via topical administration of these agents cannot be extrapolated to NSAIDS.

As such, one would not be motivated by the references to modify the formulation of Migraine Headaches to employ indomethacin.

As such, the combined teaching of Migraine Headaches in view of Geaney fails to teach or suggest topically applying an NSAID formulation to a keratinized skin surface of a head of a host as claimed.

Accordingly, Claims 1 to 28 are not obvious under 35 U.S.C. § 103(a) as over "Migraine Headaches" in view of Geaney and this rejection may be withdrawn.

CONCLUSION

The Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0815, reference no. TOPI-002CIP.

Respectfully submitted,

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By: _____

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